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(71) Applicant (*for all designated States except US*): OXFORD
GLYCOSCIENCES (UK) LTD [GB/GB]; The Forum, 86
Milton Park, Abingdon, Oxfordshire OX14 4RY (GB).

(72) Inventor; and

(75) Inventor/Applicant (*for US only*): BATES, Steven
[GB/GB]; Westhill, Aberdeenshire AB32 6XX (GB).

(74) Agent: BLAKEY, Alison, Jane; c/o Celltech R & d Lim-
ited, 208 Bath Road, Slough, Berkshire SL1 3WE (GB).

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(54) Title: TRL1 AS AN ANTIFUNGAL TARGET

(57) Abstract: The invention provides TRNA ligase (TRL1) as a novel antifungal target, screening methods for TRL1 inhibitors and their use as antifungal compounds, pharmaceutical compositions containing them and their use in medicine, specifically in the treatment of an individual susceptible to or suffering from an anti-fungal infection. In particular the compounds find use in the treat-ment of topical or mucosal (e.g. thrush and vaginal candidiasis) fungal infections, e.g. caused by fungus of the Candida species, and for systemic infections, e.g. caused by fungi of Candida and Aspergillus species, such as but not limited to C. albicans, Aspergillus flavus or Aspergillus fumigatus.

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INTERNATIONAL SEARCH REPORT

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Int. Application No
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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N33/50 C12Q1/18

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBASE, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| X | WO 02/02784 A (ANADYS PHARMACEUTICALS INC) 10 January 2002 (2002-01-10) abstract; claims 11,34 page 2, line 10 - page 7, line 16 page 34, line 1 - page 37, line 6 | 1-8 |
| X | BAYMILLER JUDITH ET AL: "Isolation and sequence of the t-RNA ligase-encoding gene of Candida albicans" GENE (AMSTERDAM), vol. 142, no. 1, 1994, pages 129-134, XP002280211 ISSN: 0378-1119 abstract | 11 |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

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Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Vanhalst, K

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Int. Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| X | PHIZICKY E M ET AL: "YEAST TRNA LIGASE MUTANTS ARE NONVIABLE AND ACCUMULATE TRNA SPLICING INTERMEDIATES" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 267, no. 7, 1992, pages 4577-4582, XP002280212 ISSN: 0021-9258 abstract | 11 |
| A | BACKER DE M ET AL: "Recent developments in molecular genetics of Candida albicans" ANNUAL REVIEW OF MICROBIOLOGY, ANNUAL REVIEWS INC., PALO ALTO, CA, US, vol. 54, 2000, pages 463-498, XP002276431 ISSN: 0066-4227 abstract | 1-8 |
| A | BACKER DE MARIANNE D ET AL: "Genomic profiling of the response of Candida albicans to itraconazole treatment using a DNA microarray" ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, AMERICAN SOCIETY FOR MICROBIOLOGY, WASHINGTON, DC, US, vol. 45, no. 6, June 2001 (2001-06), pages 1660-1670, XP002215551 ISSN: 0066-4804 abstract | 1-8 |
| A | BACKER DE M D ET AL: "An antisense-based functional genomics approach for identification of genes critical for growth of Candida albicans" NATURE BIOTECHNOLOGY, NATURE PUBLISHING, US, vol. 19, no. 3, March 2001 (2001-03), pages 235-241, XP002276432 ISSN: 1087-0156 abstract | 1-8 |
| A | BACKER DE M D ET AL: "RNA-mediated gene silencing in non-pathogenic and pathogenic fungi" CURRENT OPINION IN MICROBIOLOGY, CURRENT BIOLOGY LTD, GB, vol. 5, no. 3, June 2002 (2002-06), pages 323-329, XP002276430 ISSN: 1369-5274 abstract | 1-8 |
| A | WO 01/60975 A (BOONE CHARLES ; BUSSEY HOWARD (CA); JIANG BO (CA); ROEMER TERRY (CA);) 23 August 2001 (2001-08-23) abstract | 1-8 |

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 03/05358

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 9, 10, 12-16
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 9,10,12-16

Present claims 9,10, 12-16 relate to a compound defined by reference to a desirable characteristic or property, namely "identifiable by the method of claims 1-3 or 8".

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for no such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the methods of claims 1-3 and 8.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/05358

| Patent document cited in search report | | Publication date | Patent family member(s) | Publication date |
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| WO 0202784 | A | 10-01-2002 | US 6531289 B1 | 11-03-2003 |
| | | | CA 2408829 A1 | 10-01-2002 |
| | | | EP 1292689 A1 | 19-03-2003 |
| | | | WO 0202784 A1 | 10-01-2002 |
| WO 0160975 | A | 23-08-2001 | AU 4320401 A | 27-08-2001 |
| | | | CA 2398861 A1 | 23-08-2001 |
| | | | EP 1292668 A2 | 19-03-2003 |
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